A NON-RANDOMIZED, CONSECUTIVE ENROLLMENT EVALUATION OF THE DESolve® NOVOLIMUS ELUTING BIORESORBABLE CORONARY SCAFFOLD SYSTEM IN THE TREATMENT OF PATIENTS WITH *DE NOVO* NATIVE CORONARY ARTERY LESIONS

Elixir Medical Clinical Evaluation of the DESolve® Novolimus Eluting Bioresorbable Coronary Scaffold System

"DESolve Nx Trial – DESolve CX Arm"

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Europe

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CLINICAL STUDY SUMMARY

Trial Name and Number	DESolve Nx Trial: ELX-CL-1003
Objectives:	To evaluate the safety, performance and efficacy of the Elixir DESolve® Novolimus Eluting Bioresorbable Coronary Scaffold System (BCSS) in patients with a single *de novo* native coronary artery lesion designated the target lesion and up to one non-target lesion located in a separate epicardial vessel.
	To evaluate the performance and efficacy of the Elixir DESolve® Cx Novolimus Eluting Bioresorbable Coronary Scaffold System (BCSS) in patients with a single, de *novo* native coronary artery lesion designated the target lesion and up to one non-target lesion located in a separate epicardial vessel.
Enrollment:	The study is designed to enroll 120 non-randomized patients with a single *de novo* native coronary artery lesion designated the target lesion and up to one non-target lesion located in a separate epicardial vessel. The target lesion must measure between 2.75 mm and 3.5 mm in diameter and ≤ 10 mm or ≤ 14 mm in length able to be covered by a single 3.0 x 14, 3.0 x 18mm, 3.25 x 14 or 3.25 x 18 mm, 3.5 x 14mm or 3.5 x 18mm DESolve scaffold. As applicable, a non-target lesion located in a separate epicardial vessel must be treated first with a single, approved 'olimus drug eluting stent and if this procedure is uncomplicated and considered optimal, then the target lesion can be considered for the DESolve BCSS. The patient should not be enrolled until after satisfactory pre-dilatation of the target lesion. DESolve Cx: This study Arm is designed to enroll 30 non-randomized patients with a single, *de novo* native coronary artery lesion designated the target lesion and up to one non-target lesion located in a separate epicardial vessel. The target lesion must measure between 2.25 mm and 3.5 mm in diameter and ≤ 10 mm or ≤ 24 mm in length able to be covered by a single 2.5, 3.0, 3.25 or 3.5 mm x 14, 18 or 28 mm scaffold. The DESolve Cx is CE Mark approved and diff device differs only in the thickness of the scaffold which is 120 µm as compared to the 150 µm of

	the DESolve device previously studied and which has received CE Mark approval. As applicable, a non-target lesion located in a separate epicardial vessel must be treated first with a single, approved 'olimus drug eluting stent and if this procedure is uncomplicated and considered optimal, then the target lesion can be considered for the DESolve Cx BCSS. The patient should not be enrolled until after satisfactory pre-dilatation of the target lesion. Patients included in this DESolve Cx Arm will be enrolled at select sites.
Clinical Study Device	2.5 x 14mm, 2.5 x 18mm, 2.5 x 28mm, 3.0 x 14 mm, 3.0 x 18mm, 3.25 x 14mm and 3.25 x 18mm, 3.5 x 14mm and 3.5 x 18mm DESolve and DESolve Cx scaffolds (as available) All DESolve and DESolve Cx scaffolds are loaded with approximately 5 mcg of Novolimus per mm of scaffold length (i.e, 65 mcg on a 14mm scaffold and 85 mcg on an 18mm scaffold).
Clinical Site Locations:	Drawn from up to 15 International Sites in Brazil, Belgium, Denmark, Germany, Poland and New Zealand
Clinical Study Design	The DESolve Nx Trial is a prospective, consecutive enrolment non-randomized study designed to enroll 120 patients with a de novo lesion ≤ 14 mm in length, designated the target lesion, located in a native coronary artery with a reference vessel diameter of 2.75 mm – 3.5 mm. All patients will receive a 3.0 x 14mm, 3.25 x 14mm or 3.5 x 14 mm, 3.0 x 18 mm, 3.25 x 18mm or 3.5 x 18mm DESolve scaffold loaded with approximately 5 mcg of Novolimus per mm of scaffold length. As appropriate, a non-target lesion may be treated in a separate native epicardial vessel with a single, approved 'olimus drug eluting stent. Only the target vessel will be evaluated for the key safety and efficacy endpoints. The DESolve Cx Arm of the trial is a prospective, consecutive enrolment non-randomized study designed to up to 30 patients with a de novo lesion ≤ 14 mm in length, designated the target lesion, located in a native coronary artery with a reference vessel diameter of 2.25 mm – 3.5 mm. All patients will receive a DESolve Cx scaffold loaded with approximately 5 mcg of Novolimus per mm of scaffold length. As appropriate, a non-target lesion may be treated in a separate native epicardial vessel with a single, approved 'olimus drug eluting stent. Only the target vessel will be evaluated for the key safety and efficacy endpoints.

	Following optimal scaffold implantation, IVUS imaging will be conducted on all patients to provide information on the scaffold expansion characteristics. To provide an assessment of the lesion and scaffold morphology and scaffold strut composition over time, the following additional imaging modalities will be included: • Angiography will be completed at 6 months following the index procedure in all patients. • In a subset of the first 35 patients enrolled at select sites, IVUS and OCT will be conducted at 6 months following the index procedure. • In the DESolve Cx Arm, all patients will undergo IVUS and OCT at 6 months. • In the subset of patients enrolled at site 28 patients will undergo angiography, IVUS and OCT imaging at 36 months • Vasomotion testing will be not be required for this protocol at any time point. • Multislice computed tomography (MSCT) will be conducted at 12 months in the subset of the first 35 patients enrolled at select sites and will not be required for the DESolve Cx patients • All patients will undergo clinical follow-up at 1, 6, and 12 months and annually through 5 years. • DESolve Cx patients will undergo clinical follow-up at 1, 6, and 12 months
Clinical Endpoints:	• Clinically-indicated Major Adverse Cardiac Events (MACE) at 1, 6, and 12 months and annually to 5 years. MACE is a composite endpoint defined as cardiac death, target vessel MI, and clinically-indicated target lesion revascularization. DESolve Cx patients will undergo clinical follow-up at 1, 6, and 12 months

	• Acute Success including Device and Procedure Success • Clinically-indicated Target Lesion and Target Vessel Revascularization (CI-TLR and CI-TVR) at 1, 6, and 12 months and annually to 5 years and at 1, 6, 12 and 24 months for the DESolve Cx Arm • Clinically-indicated Target Lesion and Target Vessel Failure (CI-TLF and CI-TVF) 1, 6, and 12 months and annually to 5 years and at 1, 6, and 12 months for the DESolve Cx Arm • Scaffold Thrombosis
Angiographic Endpoints:	• All patients will undergo angiographic follow-up at 6 months. In the subset of patients enrolled at site 28, patients will undergo angiography, IVUS and OCT imaging at 36 months • In the DESolve Cx Arm all patients will undergo angiographic follow-up at 6 months The following endpoints will be analyzed: • In-scaffold late lumen loss • In-scaffold and in-lesion Binary Restenosis (≥ 50%) • In-lesion Late Lumen Loss • In-scaffold and in-segment % Diameter Stenosis • MLD and % DS post procedure • Scaffold Thrombosis • Additional parameters may be assessed • Vasomotion will not be required at any time point.
IVUS and OCT Endpoints	• To provide an assessment of the lesion and stent morphology and stent strut composition over time, the additional imaging modalities of IVUS and OCT conducted at baseline and 6 months will be completed in a subset of the first 35 patients enrolled at select sites. In the subset of patients enrolled at site 28, patients will undergo angiography, IVUS and OCT imaging at 36 months

	• In the DESolve Cx Arm all patients will undergo IVUS and OCT follow-up at 6 months The following endpoints will be analyzed: • Volumetric neointimal burden by IVUS • Changes in vessel size by IVUS • Changes in scaffold size by IVUS • Changes in strut appearance suggesting bioresorption • Incomplete scaffold apposition, acute and late, assessed by IVUS and/or Optical Coherence Tomography (OCT) • Scaffold area assessed by IVUS and/or OCT • Descriptive analysis of lesion/vessel morphometry and scaffold strut composition by OCT
MSCT **Analysis Endpoint**	In a subset of the first 35 patients enrolled at select sites, MSCT follow-up will be conducted at 12 months. The following endpoints will be analyzed: In the DESolve Cx Arm MSCT is not required • Multi-slice computed tomography (MSCT) descriptive and quantitative analysis of lesion/vessel and scaffold morphology
Treatment Strategy	• Treatment of up to two de novo native coronary artery lesions located in separate epicardial territories. One will be the target lesion and will be treated with the trial device. • Treatment of the target lesion is to be performed after optimal stenting using an approved 'olimus DES of a single non-target lesion as applicable. • To determine patient eligibility, assessment of the target vessel diameter using on-line QCA must be completed before the enrollment of the patient into the study. The target lesion is to be treated only after all clinical and angiographic inclusion criteria have been met

- Pre-dilatation of the lesion is mandatory using a balloon 0.5mm smaller than the reference vessel. If the lesion cannot be successfully pre-dilated, treatment with the DESolve CSS should not be attempted. If there is Type A dissection that cannot be covered by the DESolve CSS then the patient cannot be enrolled in the trial. Any dissection worse than Type A will preclude the patient from being enrolled into the study.

- Target lesion length should be ≤ 10 mm or ≤ 14 mm by visual estimate and have at least 2 mm of healthy vessel on either side of the lesion for coverage by the DESolve Scaffold

Table 1: Lesion length, Scaffold size and Drug dose for DESolve and DESolve Cx

Lesion length (visual estimation)	Scaffold size	Drug dose
≤ 10 mm	2.5 x 14 mm 3.0 x 14 mm 3.25 x 14mm 3.5 x 14mm	65 mcg
≤ 14 mm	2.5 x 18 mm 3.0 x 18 mm 3.25 x 18mm 3.5 x 18mm	85 mcg
≤ 24 mm	2.5 x 28 mm 3.0 x 28 mm 3.25 x 28mm 3.5 x 28mm	125 mcg

	• Bailout stenting should be conducted using any approved DES stent incorporating an "olimus" drug or bare metal stent • Patients should receive a loading dose of clopidogrel (≥ 300 mg) and aspirin (≥ 300 mg) if not currently on chronic anti-platelet therapy 24 hrs prior to the index procedure. Patients should remain on 75mg of clopidogrel daily for at least 12 months and on ≥ 75 mg of aspirin indefinitely or at least for the length of the study follow-up period of 5 years and for DESolve Cx Arm at least 2 years. • All patients will undergo angiography and IVUS post-procedurally and angiography again at the 6 month follow-up. (IVUS will only be performed at the 6-month follow-up in the 35-patient subset). • For the DESolve Cx Arm all patients will undergo angiography, IVUS and OCT at baseline and again at 6 months • IVUS and OCT will be conducted at baseline, 6 months in a subset of the first 35 patients enrolled at select sites. • In the subset of patients enrolled at site 28, patients will undergo angiography, IVUS and OCT imaging at 36 months • Vasomotor testing will not be required at any time point. • Multislice computed tomography (MSCT) will be conducted will be conducted at 12 months in the subset of the first 35 patients enrolled at select sites. • In the DESolve Cx Arm MSCT is not required
Key Inclusion Criteria	Patients have a planned intervention of up to two native coronary artery lesions located in separate epicardial territories, one designated the target lesion and the other a non-target lesion, which meet the following criteria: The non-target lesion must be treated first using a single, approved 'olimus drug eluting stent. If uncomplicated and considered optimal as defined by below, the target lesion can then be treated. Optimal treatment of non-target lesion: a. < 20% residual stenosis by visual assessment b. no evidence of dissection

	c. no evidence of thrombus in the target lesion or vessel d. TIMI 3 flow No other restrictions are placed on the non-target lesion. The patient and target lesion must meet all patient inclusion criteria and no exclusion criteria. Target Lesion inclusion criteria: • *de novo* • The target lesion reference site must be between ≥ 2.75 mm and ≤ 3.5 mm in diameter assessed by online QCA • The target vessel must be a major coronary artery or major branch with a visually estimated stenosis of ≥ 50% and <100% with TIMI flow of ≥ 1 • The visually estimated target lesion length is ≤ 10mm or ≤ 14 mm and must be able to be covered by a single 14 mm or 18 mm DESolve® Scaffold • Percutaneous intervention of lesions in a non-target vessel if: o Not part of a another clinical investigation o ≥ 30 days prior to the study index procedure o ≥ 9 months after the study index procedure (planned) o Treatment of a single, non-target lesion located in a separate major epicardial vessel (defined as LAD with septal and diagonal branches, LCX with obtuse marginal and/or ramus intermedius branches and RCA and any of its branches) attempted during the index procedure must be completed first using an approved 'olimus drug eluting stent. If the procedure is deemed uncomplicated and optimal, treatment of the target lesion with the DESolve scaffold can be considered. • Percutaneous intervention of lesions in the target vessel if: o Not part of a clinical investigation

	○ ≥ 6 months prior to the study index procedure ○ ≥ 9 months after the study index procedure (planned) ○ Previous intervention was distal to and >10mm from the target lesion • The patient must be an acceptable candidate for coronary artery bypass surgery
Key Exclusion Criteria	Patients must not have any of the following: • An untreated significant lesion of > 40% diameter stenosis remaining proximal or distal to the target site after the planned intervention • The lesion is aorto-ostial in location, an unprotected left main lesion, a lesion within 5 mm of the origin of the LAD or LCX, or involves a major side branch < 2mm in diameter • Previous placement of a stent proximal to or within 10 mm of the target lesion • Total occlusion or < TIMI 1 coronary flow in the target vessel • The proximal target vessel or target lesion contains thrombus, moderate to severe calcification or exhibits severe tortuosity (≥ 45^{o} angulation) by visual assessment • High probability that treatment other than PTCA or stenting will be required for treatment of the same lesion • Patient is a woman of childbearing potential, pregnant or nursing • Patient has received brachytherapy in an epicardial vessel • Any use of rotablator at the index procedure • The patient was diagnosed with an acute myocardial infarction within the past 72 hours and the CK and CKMB have not returned to normal and the patient is experiencing clinical symptoms indicative of ongoing ischemia

Statistical Analysis	Analysis Populations in this observational study. Modified-Intent-to-Treat Evaluable Population The modified-intent-to-treat evaluable population will consist of patients who have received the investigational device at the target lesion, who have no major procedural protocol deviations (e.g. scaffold implanted in a non-native coronary artery), no bailout scaffolding and for whom follow-up data is available. Intent-to-Treat Population The intent-to-treat population will consist of all patients enrolled in the study, regardless of the treatment actually received for the target lesion. Statistical Analyses Detailed descriptive analyses of endpoints will be performed after each follow-up time point. No effort will be made to impute or extrapolate data to replace missing values. All calculations will be based on available data with missing data excluded. Any unused or spurious data will be noted as appropriate in the final report. All clinical, angiographic, IVUS and OCT endpoints will be analyzed for the modified-intent-to-treat evaluable population. Descriptive statistics will be presented. For binary variables such as MACE, ABR, TLR, TVF, and persistent incomplete apposition of the scaffold, counts, percentages, and exact 95% confidence intervals using Clopper-Pearson's method will be calculated. For continuous variables, means, standard deviations, and 95% confidence intervals for the mean using the Gaussian approximation will be calculated. If the assumption of normality seems untenable, nonparametric summary statistics will be presented instead. For time-to-event variables, such as time to TVF, survival curves will be constructed using Kaplan-Meier estimates.